Remarks

The Final Office Action mailed 8 April 2003 has been received and reviewed. Claims 46, 49, and 50 having been amended, the pending claims are 1-50.

Claims 46, 49, and 50 have been cosmetically amended to correct an obvious grammatical error by inserting the word "selected."

Applicants note that the Examiner indicated that the pending claims are claims 1-45. Applicants respectfully submit that the pending claims are claims 1-50. Claims 46-50 were added in a Preliminary Amendment submitted by Applicants on 28 February 2002. Applicants respectfully request that claims 46-50 be entered and considered, that Figures 2, 3, and 4 be added, and that the specification be amended as requested in the Preliminary Amendment submitted by Applicants on 28 February 2002. For the Examiner's convenience, a copy of the Preliminary Amendment submitted on 28 February 2002, and related transmittal documents (including the PTO stamped return-receipt postcard) are being submitted herewith.

Reconsideration and withdrawal of the rejections are respectfully requested.

Information Disclosure Statement and Preliminary Amendment

Applicants submitted a Preliminary Amendment, an Information Disclosure Statement, 1449 forms, and the cited documents on 28 February 2002. Applicants are submitting herewith copies of the transmittal documents, along with the return-receipt postcard stamped to indicate receipt of the Preliminary Amendment, the Information Disclosure Statement, the 1449 forms, and the cited documents by the United States Patent and Trademark Office. In the interest of expediting prosecution of the present application, Applicants are submitting, for the Examiner's convenience, courtesy copies of the Preliminary Amendment, the Information Disclosure Statement, the 1449 forms, and the cited documents. Applicants do not believe that any fee is necessary, as the Information Disclosure Statement was submitted prior to the mailing of the first Office Action on the merits, as documented by the stamped, return-receipt postcard.

However, if the Examiner believes a fee is necessary, please charge Deposit Account No. 13-4895. Consideration of each of the documents listed on the attached 1449 form(s) is respectfully requested. Pursuant to the provisions of M.P.E.P. §609, Applicants further request that a copy of the 1449 form(s), marked as being considered and initialed by the Examiner, be returned with the next Official Communication

Rejection under 35 U.S.C. §103

The Examiner rejected claims 1, 5-16, 20, and 23 under 35 U.S.C. §103(a) as being unpatentable over Park et al. (U.S. Patent No. 5,861,251) in view of Shultz et al. (U.S. Patent No. 6,242,235 B1) and Hayes et al. (U.S. Patent No. 5,721,123).

> "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure."

M.P.E.P. §706.02(j) citing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Independent claim 1 (as well as independent claims 17, 18, and 19, which are not subject to this rejection) recites that a "dye inactivates the enzyme in the absence of the surfactant." Independent claim 20 (as well as independent claim 24, which is not subject to this rejection) recites the presence of a dye "under conditions that normally inactivate the enzyme." Applicants respectfully submit Park et al. in view of Shultz et al. and Hayes et al. fail to teach or suggest all the claim language including, for example, a composition in which a "dye inactivates the enzyme in the absence of the surfactant" (e.g., claims 1-19), or a method of stabilizing an

enzyme in the presence of a dye "under conditions that normally inactivate the enzyme," wherein the method includes "combining an effective amount of a . . . surfactant . . . with the enzyme and the dye (e.g., claims 20-24). Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness.

PARK ET AL. FAIL TO SUGGEST OR DISCLOSE A PCR REAGENT MIXTURE THAT INCLUDES THE COMBINATION OF A POLYMERASE, A DYE, AND A NONIONIC SURFACTANT

"A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." M.P.E.P. §2141.02, citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

For support of the rejection of claims 1, 5-16, 20, and 23 under 35 U.S.C. §103(a), the Examiner alleged that Park et al. "disclose a PCR reagent mixture containing a polymerase, a dye and a nonionic surfactant" (page 3, lines 13-14, of the Office Action mailed 8 April 2003), and pointed to column 3, lines 1-30 of Park et al. for specific support. Applicants respectfully disagree with the Examiner's characterization of Park et al.

Applicants note that the word "dye" does not even appear in column 3, lines 1-30 of Park et al. *Further, Applicants Representatives respectfully submit that no where in the specification of Park et al. is there a disclosure of a PCR reagent mixture containing the combination of a polymerase, a dye, and a nonionic surfactant.* The specification of Park et al. recites a disjointed collection of species that may be included in a reagent for PCR. Applicants respectfully submit that the Examiner is improperly picking and choosing individually disclosed species to arrive at the presently claimed combination, with no disclosure from Park et al. to guide one of skill in the art to arrive at the presently claimed combination.

Specifically, Park et al. disclose that a "reagent for PCR . . . is prepared by freeze-drying a conventional aqueous reaction mixture which consists of a reaction buffer, $MgCl_2$, dNTPs and a DNA polymerase" (column 3, lines 3-7). "The PCR reagent of the invention may further comprise a sedimenting agent or a water-soluble dye in the presence/absence of stabilizer" (column 3, lines 30-32). Thus, Park et al. clearly disclose a PCR reagent mixture containing the combination of a polymerase; a sedimenting agent *or* a water-soluble dye; and, optionally, a stabilizer.

The Examiner also alleged that "Park et al clearly teach that the dye can be used in the presence/absence of the *stabilizer which can be the surfactant* (col 3, lines 30-35)" (page 4, lines 16-18, of the Office Action mailed 8 April 2003, emphasis added). Applicants respectfully disagree with the Examiner's characterization of Park et al.

The only recitation of the term *surfactant* by Park et al. is the isolated recitation that it has been well known that "non-ionic surfactants . . . improve the reactivity of the PCR mixture" (column 3, lines 18-20). However, Park et al. fail to disclose or suggest including such non-ionic surfactants in their disclosed PCR mixtures. Further, Park et al. clearly draw a distinction (e.g., column 3, lines 16-20) between materials that *stabilize a DNA polymerase and dNTPs* (e.g., "gelatin, BSA, Thesit (polyoxyethylene-9-lauryl ether), PEG-8000 (polyethyleneglycol-8000) or polyol (e.g., glycerol, glucose, mannitol, galacitol, glucitol and sorbitol)" as recited at column 3, lines 24-27) and *materials that improve the reactivity of a PCR mixture* (e.g., "non-ionic surfactants such as NP40 and Tween 20 etc. as recited at column 3, lines 18-20), thereby teaching away from the possibility that a stabilizer might function as a non-ionic surfactant. Park et al. also fail to provide guidance to one of skill in the art to select from the list of 10 recited stabilizers (e.g., gelatin, BSA, Thesit, PEG-8000, glycerol, glucose, mannitol, galacitol, glucitol, and sorbitol) a stabilizer that, although not disclosed as such, might function as a non-ionic surfactant (e.g., Thesit).

Moreover, although Park et al. disclose the combination of a polymerase, a sedimenting agent or a water-soluble dye, in the presence/absence of stabilizer, they provide no guidance for one of skill in the art to (i) select a *dye* from the choice of *a dye or a sedimenting agent* (1 out of 2 choices), and (ii) select a stabilizer that, although not disclosed as such, might function as *a non-ionic surfactant* (e.g., Thesit) from the possibility of no stabilizer or one of the ten listed stabilizers (1 out of 11 choices) to arrive at *the combination of a polymerase, a dye, and a nonionic surfactant* (1 out of 22 choices).

SCHULTZ ET AL. FAIL TO DISCLOSE OR SUGGEST COMPOSITIONS THAT INCLUDE A DYE

Shultz et al. disclose "methods and compositions for protein stabilization, particularly the stabilization of polymerases in aqueous solutions with cationic surfactants. The activity of polymerases in solution, either in storage buffers or reaction buffers, may be stabilized by the addition of non-ionic surfactants" (column 6, lines 38-43). However, Shultz et al. fail to teach or suggest, among other things, any methods or compositions that include a dye. Thus, Schultz et al. also fail to teach or suggest stabilization of compositions that include a dye with non-ionic surfactants.

HAYES ET AL. FAIL TO DISCLOSE OR SUGGEST COMPOSITIONS THAT INCLUDE A SURFACTANT

Hayes et al. disclose "methods and apparatus for changing the temperature of material in a vessel by exposing the vessel to electromagnetic radiation" (column 1, lines 5-8). Hayes et al. further disclose the use of "heat absorptive dyes . . . for enhancing the heating effect of the electromagnetic radiation" (column 3, lines 10-12). However, Hayes et al. fail to teach or suggest, among other things, any methods or apparatuses that include a surfactant.

ONE OF SKILL IN THE ART WOULD HAVE NO MOTIVATION TO COMBINE PARK ET AL. IN VIEW OF SCHULTZ ET AL. AND HAYES ET AL. TO ARRIVE AT THE PRESENTLY CLAIMED INVENTION

Although documents can be combined in order to determine obviousness, "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988). One cannot simply "engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps." *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). Further, both the suggestion for combining the teachings of the prior art to make the invention and the reasonable likelihood of its success must be founded in the prior art and not in the teachings of Applicants' disclosure. *In re Dow Chem. Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Applicants respectfully submit that the cited art neither suggests the combination of its teachings nor suggests the reasonable likelihood that such a combination would result in the presently claimed invention.

First, the Examiner alleged that "[i]t would have been obvious to include in the PCR reagent mixture of Park et al a nonionic surfactant to obtain its function to improve reactivity as taught by Park et al and to obtain its function to stabilize the polymerase as taught by Schultz et al." (page 3, lines 21-24, of the Office Action mailed 8 April 2003). Applicants respectfully traverse the Examiner's allegation. Applicants respectfully submit that, absent hindsight reconstruction, one of skill in the art would have no motivation to combine Park et al. with Schultz et al., to arrive at the presently claimed invention. For example, the present invention recites a composition in which a "dye inactivates the enzyme in the absence of the surfactant" (e.g., claims 1-19), or a method of stabilizing an enzyme in the presence of a dye "under conditions that normally inactivate the enzyme," wherein the method includes "combining an effective amount of a . . . surfactant . . . with the enzyme and the dye" (e.g., claims 20-24).

Applicants respectfully submit that one of skill in the art would have no motivation to combine Schultz et al., which fails to disclose or suggest stabilization of compositions that include a dye with non-ionic surfactants, with Park et al., which discloses dye-containing compositions. Further, Applicants respectfully submit that one of skill in the art would not have a reasonable expectation of success in combining Park et al. with Schultz et al. to stabilize an enzyme in the presence of a dye.

Second, the Examiner alleged that "[i]t would have been further obvious to include in the reagent mixture a heat absorptive dye to obtain its function of enhancing the heating effect of electromagnetic radiation as taught by Hayes et al. (page 3, line 24 to page 4, line 2, of the Office Action mailed 8 April 2003). Applicants respectfully traverse the Examiner's allegation. Applicants respectfully submit that, absent hindsight reconstruction, one of skill in the art would have no motivation to combine Park et al. in view of Schultz et al. with Hayes et al., to arrive at the presently claimed invention. Further, Applicants respectfully submit that Hayes et al., which fails to disclose or suggest any methods or apparatuses that include a surfactant, fail to correct the deficiencies of Park et al. in view of Schultz et al.

Finally, the Examiner alleged that "the dye of Park et al and/or the heat absorptive dye of Hayes et al would have *inherently* reduced polymerase activity in the absence of the surfactant" (page 4, lines 11-13, of Office Action mailed 8 April 2003, emphasis added). Applicants respectfully traverse the Examiner's allegation. Applicants respectfully reiterate that that Park et al., do not disclose, and in fact teach away from, a composition in which a "dye inactivates the enzyme in the absence of the surfactant" (e.g., claims 1-19), or a method of stabilizing an enzyme in the presence of a dye "under conditions that normally inactivate the enzyme," wherein the method includes "combining an effective amount of a . . . surfactant . . . with the enzyme and the dye" (e.g., claims 20-24). *See, for example*, the arguments in the paragraph spanning pages 6-7 of the Amendment and Response submitted by Applicants on 15 January 2003, which is incorporated herein by reference. The Examiner responded by asserting

that "Applicants may be using a different method for determining a decrease in enzyme activity due to the dye than used by Park et al for determining a decrease in PCR level." Applicants respectfully submit that the Examiner's response is not relevant to the present fact situation. No matter what method of measurement was used, Park et al., in referring to PCR compositions including dyes, stated that "there was no decrease in the level of PCR" (column 6, lines 16-17). Applicants respectfully submit that this is evidence that Park et al. do not disclose a composition in which a "dye inactivates the enzyme in the absence of the surfactant" (e.g., present claims 1-19), or a method of stabilizing an enzyme in the presence of a dye "under conditions that normally inactivate the enzyme" (e.g., claims 20-24).

Applicants respectfully submit that Park et al. in view of Shultz et al. and Hayes et al. fail to teach or suggest the presently claimed invention. Furthermore, Park et al., Shultz et al., and Hayes et al. provide no suggestion or motivation for one of skill in the art to modify or to combine their teachings to arrive at the present invention with a reasonable expectation of success.

The Examiner rejected claims 2-4, 17-19, 21, and 24 under 35 U.S.C. §103(a) as being unpatentable over Park et al. (U.S. Patent No. 5,861,251) in view of Shultz et al. (U.S. Patent No. 6,242,235 B1) and Hayes et al. (U.S. Patent No. 5,721,123) as applied to claims 1, 5-16, 20, and 23, and further in view of Nadeau et al. (U.S. Patent No. 5,919,630).

The deficiencies of Park et al. in view of Shultz et al. and Hayes et al., as applied to claims 1-24, have been discussed herein above.

Nadeau et al. disclose "methods for detecting nucleic acid target sequences" (column 1, lines 9-10). However, Nadeau et al. fail to disclose or suggest, among other things, any methods that include a surfactant. Thus, Nadeau et al. provide nothing to correct the deficiencies of Park et al. in view of Shultz et al. and Hayes et al. Furthermore, Applicants respectfully submit that one cannot simply engage in a hindsight reconstruction of the claimed

invention, using Applicants' structure as a template and selecting elements from documents to fill the gaps.

Based on the remarks presented herein above, Applicants respectfully submit that claims 2-4, 17-19, 21, and 24 are patentable over Park et al. in view of Shultz et al. and Hayes et al., and further in view of Nadeau et al.

Applicants respectfully request that the rejections under 35 U.S.C. §103(a) be reconsidered and withdrawn.

Obviousness-Type Double Patenting Rejection

Claims 1-24 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-45 of copending Application No. 09/841,272. Upon an indication of otherwise allowable subject matter and in the event this rejection is maintained, Applicants will provide an appropriate response.

If the provisional obviousness-type double patenting rejection is the only rejection remaining in this application, the Examiner is requested to withdraw the rejection and permit the application to issue as a patent, thereby allowing any such issues to be resolved in the issuance of the other application. M.P.E.P. §804 affirmatively directs the Examiner to withdraw the provisional obviousness-type double patenting rejection under such circumstances.

Reconsideration and withdrawal of the provisional obviousness-type double patenting rejection are respectfully requested.

Request for Rejoinder

Claims 25-45 have been withdrawn by the Examiner from further consideration as being drawn to a non-elected invention. Reconsideration and withdrawal of the restriction requirement is respectfully requested. Applicants respectfully note that a response with traverse is not a condition precedent for the Examiner to reconsider a Restriction Requirement. Although

per M.P.E.P. §818.03, an Applicant must traverse to preserve the right of petition. Applicants Representatives are not aware of any authority for prohibiting reconsideration of a restriction requirement by an Examiner at any time during the prosecution.

In the event the Examiner maintains the restriction requirement, rejoinder of the non-elected claims is respectfully requested upon notice of allowable subject matter. Notably, all the independent claims that have been withdrawn from further consideration (e.g., claims 25, 31, 41, and 45), are method claims that recite the language of the composition of, for example, independent claim 1. Similarly independent claim 46 is a device claim that recites the language of the composition of, for example, independent claim 1; and independent claims 49 and 50 are method claims that recite the language of the composition of, for example, independent claim 1. *See* 1184 O.G. 86 citing *In re Ochiai*, 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1996). Applicants respectfully note that a response with traverse is not a condition precedent for the Examiner to rejoin restricted claims. *See, for example*, M.P.E.P. §821.02, entitled *After Election Without Traverse*, which states that "where the application contains an allowed generic claim, and applicant has not been previously notified as to the allowance of a generic claim, the examiner *must*, prior to canceling the nonelected claims, notify applicant of the allowance of a generic claim and give applicant a time limit of 1-month (not less than 30 days) to conform all of the claims to the nonelected species to fully embrace an allowed generic claim." (emphasis added).

Claims 46-50

Independent claim 46 recites a device for use in thermal processing, the device comprising: a substrate comprising first and second major surfaces; a plurality of process chambers in the device, each of the process chambers defining a volume for containing a sample mixture; a plurality of valves with at least one of the valves located between selected pairs

of the process chambers; and wherein the sample mixture comprises an enzyme, a dye, and an effective amount of a surfactant selected from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, wherein the dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits such interaction. Claims 47-48 depend from claim 46.

Independent claim 49 recites a method of conducting a thermal cycling process comprising: providing a device comprising a plurality of process chambers, each of the process chambers defining a volume for containing a sample mixture; providing a sample mixture in at least some of the process chambers; delivering electromagnetic energy to the process chambers to raise the temperature of the sample mixture in the process chambers; rotating the device about an axis of rotation while delivering the electromagnetic energy, wherein the temperature of the sample mixture in the process chambers is controlled as the substrate rotates; and wherein the sample mixture comprises an enzyme, a dye, and an effective amount of a surfactant selected from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, wherein the dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits such interaction.

Independent claim 50 recites a method of processing sample material comprising: providing a device comprising a plurality of process chamber arrays, each of the process chamber arrays comprising a loading chamber, a first process chamber, and a second process chamber; providing a sample mixture in the loading chamber of at least one of the process chamber arrays; moving the sample mixture from the loading chamber into the first process chamber by rotating the device; controlling the temperature of the sample mixture in the first process chamber by rotating the device about an axis of rotation while delivering electromagnetic energy to the first process chamber; moving the sample mixture from the first process chamber to the second process chamber by rotating the device; controlling the temperature of the sample mixture in the second process chamber by rotating the device about an axis of rotation while delivering electromagnetic energy to the second process chamber; and wherein the sample mixture

comprises an enzyme, a dye, and an effective amount of a surfactant selected from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, wherein the dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits such interaction.

Claims 46-50 were presented by Applicants before the first Official Action by the United States Patent and Trademark Office. However, claims 46-50 have not been considered by the Examiner. Applicants respectfully request full and fair consideration of each of claims 46-50, along with the appropriate opportunity to respond to any rejections of claims 46-50.

Summary

It is respectfully submitted that all the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

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CERTIFICATE UNDER 37 CFR §1.10:
"Express Mail" mailing label number: EV 073 735 572 US Date of Deposit: 30 June 2003
The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, **Mail Stop AF**, P.O. Box 1450, Alexandria, VA 22313-1450.

By: _____
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APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 09/841,264
Docket No.: 56286US003

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been marked in bold typeface.

In the Claims

For convenience, all pending claims are shown below.

1. A composition comprising an enzyme, a dye, and an effective amount of a surfactant selected from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, wherein the dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits such inactivation.

2. The composition of claim 1 wherein the dye is selected from the group of a near-IR dye, a uv/visible dye, a fluorescent dye, and a mixture thereof.

3. The composition of claim 2 wherein the dye is a near-IR dye.

4. The composition of claim 3 wherein the near-IR dye is a diimminium dye or a cyanine dye.

5. The composition of claim 1 wherein the enzyme is a polymerase or a ligase.

6. The composition of claim 1 wherein the nonionic surfactant is selected from the group of esters of fatty acids and polyhydric alcohols, fatty acid alkanolamides, ethoxylated fatty acids, ethoxylated aliphatic acids, ethoxylated fatty alcohols, ethoxylated aliphatic alcohols, ethoxylated sorbitol fatty acid esters, ethoxylated glycerides, ethoxylated block copolymers with EDTA, ethoxylated cyclic ether adducts, ethoxylated amide and imidazoline adducts, ethoxylated

amine adducts, ethoxylated mercaptan adducts, ethoxylated condensates with alkyl phenols, ethoxylated nitrogen-based hydrophobes, ethoxylated polyoxypropylenes, polymeric silicones, fluorinated surfactants, polymerizable surfactants, and mixtures thereof.

7. The composition of claim 1 wherein the zwitterionic surfactant is selected from the group of alkylamido betaines and amine oxides thereof, alkyl betaines and amine oxides thereof, sulfo betaines, hydroxy sulfo betaines, amphoglycinates, amphopropionates, balanced amphopolycarboxyglycinates, and alkyl polyaminoglycinates, and mixtures thereof.

8. The composition of claim 1 wherein the dye is present at a concentration of at least about 0.005 mg/mL.

9. The composition of claim 1 wherein the effective amount of surfactant is at least about 0.5 wt-%.

10. The composition of claim 9 wherein the effective amount of surfactant is no greater than about 20 wt-%.

11. The composition of claim 1 further comprising a buffer.

12. The composition of claim 1 further comprising a triphosphate.

13. The composition of claim 1 further comprising a reference dye.

14. The composition of claim 1 further comprising an antioxidant.

15. The composition of claim 14 wherein the dye is capable of optical degradation.

16. The composition of claim 1 wherein the surfactant is an antioxidant.

17. A composition comprising a polymerase enzyme, a near-IR dye, and an effective amount of a surfactant selected from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, wherein the near-IR dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits the inactivation.

18. A composition comprising:

a polymerase enzyme;

a near-IR dye selected from the group of a diimminium dye, a cyanine dye, and a mixture thereof; and

an effective amount of a nonionic surfactant;

wherein the near-IR dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits the inactivation.

19. A composition comprising:

a polymerase enzyme;

a near-IR dye selected from the group of a diimminium dye, a cyanine dye, and a mixture thereof; and

an effective amount of a nonionic surfactant selected from the group of esters of fatty acids and polyhydric alcohols, fatty acid alkanolamides, ethoxylated fatty acids, ethoxylated aliphatic acids, ethoxylated fatty alcohols, ethoxylated aliphatic alcohols, ethoxylated sorbitol fatty acid esters, ethoxylated glycerides, ethoxylated block copolymers with EDTA, ethoxylated cyclic ether adducts, ethoxylated amide and imidazoline adducts, ethoxylated amine adducts,

ethoxylated mercaptan adducts, ethoxylated condensates with alkyl phenols, ethoxylated nitrogen-based hydrophobes, ethoxylated polyoxypropylenes, polymeric silicones, fluorinated surfactants, polymerizable surfactants, and mixtures thereof;

wherein the near-IR dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits the inactivation.

20. A method of stabilizing an enzyme in a fluid sample in the presence of a dye under conditions that normally inactivate the enzyme, the method comprising combining an effective amount of a surfactant selected from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, with the enzyme and the dye, wherein the surfactant inhibits inactivation of the enzyme.

21. The method of claim 20 wherein the dye is selected from the group of a near-IR dye, a uv/visible dye, a fluorescent dye, and a mixture thereof.

22. The method of claim 21 wherein the enzyme is a polymerase or a ligase.

23. The method of claim 20 wherein the surfactant is a nonionic surfactant selected from the group of esters of fatty acids and polyhydric alcohols, fatty acid alkanolamides, ethoxylated fatty acids, ethoxylated aliphatic acids, ethoxylated fatty alcohols, ethoxylated aliphatic alcohols, ethoxylated sorbitol fatty acid esters, ethoxylated glycerides, ethoxylated block copolymers with EDTA, ethoxylated cyclic ether adducts, ethoxylated amide and imidazoline adducts, ethoxylated amine adducts, ethoxylated mercaptan adducts, ethoxylated condensates with alkyl phenols, ethoxylated nitrogen-based hydrophobes, ethoxylated polyoxypropylenes, polymeric silicones, fluorinated surfactants, polymerizable surfactants, and mixtures thereof.

24. A method of stabilizing a polymerase enzyme in solution in the presence of a near-IR dye under conditions that normally inactivate the enzyme, the method comprising combining an effective amount of a nonionic surfactant with the enzyme and the dye, wherein the surfactant inhibits inactivation of the enzyme.

25. A method of conducting a thermal process, the method comprising:

providing a sample mixture comprising a biological material, an enzyme, an effective amount of a surfactant selected from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, and a dye at a first temperature; and

directly heating the sample mixture to a second temperature higher than the first temperature;

wherein the dye inactivates the enzyme in the absence of the surfactant and the surfactant inhibits the inactivation.

26. The method of claim 25 further comprising cooling the sample mixture and directly reheating the sample mixture in a thermal cycling process.

27. The method of claim 26 wherein the thermal cycling process comprises at least about 25 cycles.

28. The method of claim 27 wherein the first temperature is within a range of about 0°C to about 50°C.

29. The method of claim 27 wherein the second temperature is within a range of about 50°C to about 95°C.

30. The method of claim 27 wherein the thermal cycling process comprises heating between a temperature of about 50°C and about 95°C.

31. A method of conducting a thermal cycling process, the method comprising:

providing a device comprising at least one process chamber that defines a volume for containing a sample mixture comprising a biological material, an enzyme, a dye, and an effective amount of a surfactant selected from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof;

delivering electromagnetic energy to the process chamber to raise the temperature of the sample material in the process chamber, wherein the dye converts the electromagnetic energy into thermal energy;

wherein the dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits such inactivation.

32. The method of claim 31 wherein the dye is a near-IR dye.

33. The method of claim 31 wherein the surfactant is a nonionic surfactant selected from the group of esters of fatty acids and polyhydric alcohols, fatty acid alkanolamides, ethoxylated fatty acids, ethoxylated aliphatic acids, ethoxylated fatty alcohols, ethoxylated aliphatic alcohols, ethoxylated sorbitol fatty acid esters, ethoxylated glycerides, ethoxylated block copolymers with EDTA, ethoxylated cyclic ether adducts, ethoxylated amide and imidazoline adducts, ethoxylated amine adducts, ethoxylated mercaptan adducts, ethoxylated condensates with alkyl phenols, ethoxylated nitrogen-based hydrophobes, ethoxylated polyoxypropylenes, polymeric silicones, fluorinated surfactants, polymerizable surfactants, and mixtures thereof.

34. The method of claim 31 wherein the sample mixture further comprises an antioxidant.

35. The method of claim 31 wherein the surfactant is present in an amount of at least about 0.5 wt-%.

36. The method of claim 35 wherein the surfactant is present in an amount of no greater than about 20 wt-%.

37. The method of claim 31 wherein the sample mixture further comprises a buffer.

38. The method of claim 31 wherein the sample mixture further comprises a triphosphate.

39. The method of claim 31 wherein the sample mixture further comprises a reference dye.

40. The method of claim 31 wherein the enzyme is a polymerase or a ligase.

41. A method of conducting a thermal cycling process comprising:

providing a device comprising at least one process chamber that defines a volume for containing a sample mixture comprising a biological material, a polymerase enzyme, a near-IR dye, an effective amount of a nonionic surfactant, and a triphosphate;

delivering electromagnetic energy to the process chamber to raise the temperature of the sample material in the process chamber, wherein the dye converts the electromagnetic

energy into thermal energy;

wherein the dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits such inactivation.

42. The method of claim 41 further comprising cooling the sample mixture and reheating the sample mixture in a thermal cycling process.

43. The method of claim 42 wherein the thermal cycling process comprises at least about 25 cycles.

44. The method of claim 42 wherein the thermal cycling process comprises heating between a temperature of about 50°C and about 95°C.

45. A method of denaturing hydrogen-bonded molecules, the method comprising:

providing a sample mixture comprising hydrogen-bonded molecules, an enzyme, an effective amount of a surfactant selected from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, and a dye at a first temperature; and

directly heating the sample mixture to a second temperature higher than the first temperature effective to denature the hydrogen-bonded molecules;

wherein the dye inactivates the enzyme in the absence of the surfactant and the surfactant inhibits the inactivation.

46. **(Amended)** A device for use in thermal processing, the device comprising:

a substrate comprising first and second major surfaces;

a plurality of process chambers in the device, each of the process chambers defining a volume for containing a sample mixture;

a plurality of valves with at least one of the valves located between selected pairs of the process chambers: and

wherein the sample mixture comprises an enzyme, a dye, and an effective amount of a surfactant **selected** from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, wherein the dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits such interaction.

47. The device of claim 46 wherein each valve comprises an impermeable disc distinct from the substrate, wherein the impermeable disc of each of the valves separates the selected pairs of process chambers.

48. The device of claim 46 further comprising:

a baffle structure on the first major surface of the substrate, wherein airflow over the first major surface is disrupted when the substrate is rotated.

49. **(Amended)** A method of conducting a thermal cycling process comprising:

providing a device comprising a plurality of process chambers, each of the process chambers defining a volume for containing a sample mixture;

providing a sample mixture in at least some of the process chambers;

delivering electromagnetic energy to the process chambers to raise the temperature of the sample mixture in the process chambers;

rotating the device about an axis of rotation while delivering the electromagnetic energy, wherein the temperature of the sample mixture in the process chambers is controlled as the substrate rotates; and

wherein the sample mixture comprises an enzyme, a dye, and an effective amount of a surfactant **selected** from the group of a nonionic surfactant, a zwitterionic surfactant, and a

mixture thereof, wherein the dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits such interaction.

50. **(Amended)** A method of processing sample material comprising:

providing a device comprising a plurality of process chamber arrays, each of the process chamber arrays comprising a loading chamber, a first process chamber, and a second process chamber;

providing a sample mixture in the loading chamber of at least one of the process chamber arrays;

moving the sample mixture from the loading chamber into the first process chamber by rotating the device;

controlling the temperature of the sample mixture in the first process chamber by rotating the device about an axis of rotation while delivering electromagnetic energy to the first process chamber;

moving the sample mixture from the first process chamber to the second process chamber by rotating the device;

controlling the temperature of the sample mixture in the second process chamber by rotating the device about an axis of rotation while delivering electromagnetic energy to the second process chamber; and

wherein the sample mixture comprises an enzyme, a dye, and an effective amount of a surfactant **selected** from the group of a nonionic surfactant, a zwitterionic surfactant, and a mixture thereof, wherein the dye inactivates the enzyme in the absence of the surfactant, and the surfactant inhibits such interaction.